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(71) Applicant (for all designated States except US): **HER MAJESTY IN RIGHT OF CANADA** As represented By the **MINISTER OF AGRICULTURE AND AGRI-FOOD CANADA** [CA/CA]; Agriculture and Agri-food Canada, Saskatchewan Research Centre, 107 Science Place, Saskatoon, Saskatchewan S7N 0X2 (CA).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **ROZWADOWSKI,**

**Kevin, L.** [CA/CA]; 86 Harvard Crescent, Saskatoon, Saskatchewan S7N 3R1 (CA). **LYDIATE, Derek, J.** [GB/CA]; 101 Albert Street, Saskatoon, Saskatchewan S7N 1E6 (CA).

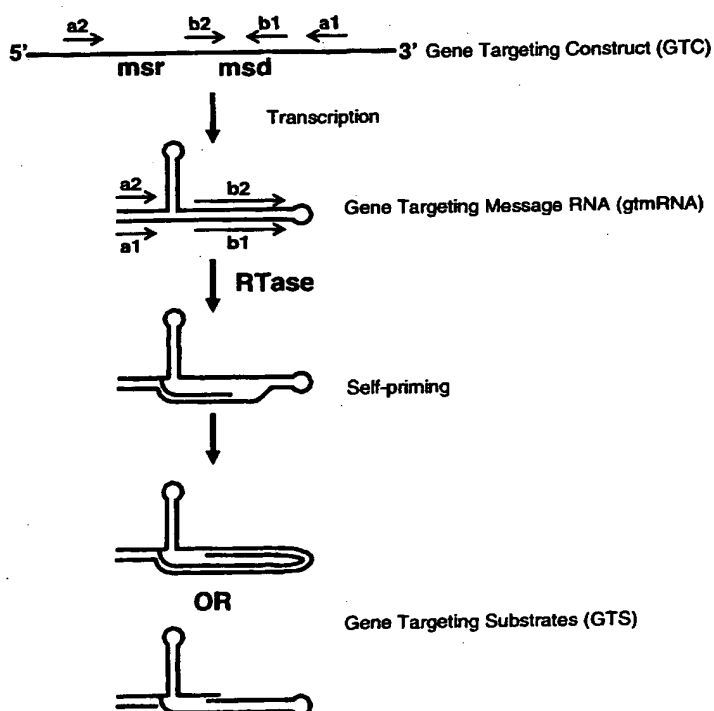
(74) Agents: **Kingwell, Brian, G.** et al.; Smart and Biggar Box 11560, Vancouver 650 West Georgia Street, Suite 2200 Vancouver, British Columbia V6B 4N8 (CA).

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(54) Title: **RETRONS FOR GENE TARGETING**



(57) Abstract: The invention provides methods and nucleic acid constructs that may be used to modify a nucleic acid of interest at a target locus within the genome of a host. In some aspects, the invention contemplates producing *in vivo* a gene targeting substrate (GTS), which may be comprised of both DNA and RNA components. The gene targeting substrate may comprise a gene targeting nucleotide sequence (GTNS), which is homologous to the target locus, but comprises a sequence modification compared to the target locus. The gene targeting substrate may be produced by reverse transcription of a gene targeting message RNA (gtmRNA). The gene targeting message RNA may be folded for self-priming for reverse transcription by a reverse transcriptase. The gene targeting message RNA may in turn be the product of transcription of a gene targeting construct (GTC) encoding the gene targeting message RNA. The gene targeting construct may for example be a DNA sequence integrated into the genome of the host, or integrated into an extrachromosomal element. Following expression of the gene targeting systems of the invention, hosts may for example be selected having genomic modifications at a target locus that correspond to the sequence modification present on the gene targeting nucleotide sequence.

In some embodiments, the structure of retrons may be adapted for use in the gene targeting systems of the invention.